



Access to Medicines in Latin America and the Caribbean (LAC): a scoping study

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Access to Medicines in Latin America and the Caribbean (LAC): a scoping study

Running title: Scoping study on access to medicines

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Abstract

Objective: To assess scientific publication trends on ATM in Latin America and the Caribbean (LAC) low and middle income countries (LMIC) and to map research gaps, focusing on methodological approaches used to study ATM, institutions and countries involved as well as the main issues raised by authors.

Search strategy: A scoping study of the scientific literature on ATM was performed, on Medline, ISI, SCOPUS and Lilacs databases, covering the fields of health, social sciences and humanities, from 2000 to 2010.

Selection criteria: Research articles and reviews published in English, Spanish and Portuguese were included. Studies including only high-income countries were excluded, as well as those carried out in very limited settings and discussion papers.

Data extraction: The 77 articles retained were categorized through consensus among authors according to the level of the health system addressed, ATM domain and research issues covered.

Results: An increasing number of publications were found ($r\ 0.93$, $p=0.00$; $R^2\ 0.85$). The top five countries covered were Brazil (68.8%), Mexico (15.6%), Colombia (11.7%), Argentina (10.4%) and Peru (10.4%). 'Health services delivery' and 'Patients, household and communities' were the health system levels most frequently addressed. Regarding ATM Domains, 'Leadership and governance', 'Sustainable financing, affordability and price of medicines', 'Medicines selection and use' and 'Availability of medicines' were the top four explored. There are research gaps in important areas, such as 'Human resources for health', 'Global policies and human rights', 'Production of medicines' and 'Traditional medicine'.

Conclusions: The upward trend on scientific publication reflects a growing research capacity in the region, which is concentrated in a few countries and research themes. The gaps on research capacity could be overcome through research collaboration among countries. It is important to strengthen these collaborations, assuring that interests and needs from the LMIC are addressed and local capacity building is promoted.

Key words Access to medicines; Bibliometrics; Scoping study; Low and middle-income countries; Latin America; Caribbean region.

ARTICLE SUMMARY

Article focus

- To identify methodological approaches and research issues on published papers, which address access to medicines (ATM) in Latin American and the Caribbean (LAC).
- To learn about LAC researchers' capacity to produce evidence on ATM through articles published on peer-reviewed journals.
- To identify research gaps on ATM that should be addressed in future studies.
- To map potential opportunities for south-south collaboration on ATM research.

Key messages

- An increasing trend on scientific publications on ATM reflects a growing research capacity in LAC.
- Scientific publications in peer-reviewed journals are concentrated in few countries and on well-established areas and themes.
- 'Health services delivery' and 'Patients, household and communities' were the health system levels most frequently addressed.
- Regarding ATM Domains, 'Leadership and governance', 'Sustainable financing, affordability and price of medicines', 'Medicines selection and use' and 'Availability of medicines' were the top four explored.

Strengths and Limitations

- Local databases in Spanish and in Portuguese, the main languages in the region, which are generally not covered in other similar studies, were searched.
- It was not performed quality assessment of the papers retained.

Introduction

Access to medicines is a key component of the health care systems. The provision of regular access to affordable, appropriate and high-quality medicines has been established as a global priority set out on several international commitments such as the World Health Assembly's resolutions [1-4], the Millennium Development Goals [5], UNGASS declarations [6 7], the Oslo Declaration [8] and the Political Declaration on HIV and AIDS: Intensifying Our Efforts to Eliminate HIV and AIDS [9]. In line with these commitments, governments of many Low and Middle Income Countries (LMIC) have been implementing access to medicines related policies.

Scaling-up access to medicines in developing countries has been a major challenge faced by these countries' governments and health authorities. The delivery of medicines to most people in need depends on a series of efforts related to different access components or dimensions such as, sustainable financing, the existence of a network of reliable health services, and an efficient supply chain management [10].

In this context, the existence of reliable and accurate information on the different components of the access to medicines is crucial to better understanding, planning and developing those policies. Despite the growing number of studies on issues like price and availability [11], quality data on access to and use of medicines are still lacking [12 13]. This turns it difficult to build a culture of evidence based decision making in LMICs.

This work is part of activities carried out within the Access to Medicines (ATM) policy research program, recently implemented by the Alliance for Health Policy and System Research (AHPSR) [14].

This paper aims to assess scientific publication trends on Access to Medicines in Latin America and the Caribbean (LAC) and to map research gaps.

Methods

A scoping study [15 16] of the scientific literature on access to medicines was performed covering ten years: January 2000 to September 2010. This review was intended to map scientific production on access to medicines related topics in LAC focusing on

methodological approaches used to study access to medicines, institutions and countries involved as well as the main issues raised by authors.

Databases searched were: Medline, ISI, SCOPUS and Lilacs, intending to cover publications on ATM in the in the fields of health, social sciences and humanities. Search terms were set and combined according to the database features (Box 1).

The articles identified were screened and selected according to inclusion criteria, as follows: focus on access to medicines; address at least one low or middle-income country (LMIC) or LMIC regions (districts, provinces, states); text in English, Spanish and Portuguese; abstract available; full-text available on open-access journals and on *Periódicos CAPES* e-journals database; and empiric or reviews articles. For review articles, some additional inclusion criteria applied: it must include information on how the literature search was done and which scientifically recognized index was used; selection criteria must define the type of articles accepted. Exclusion criteria were: studies including only high-income countries; empirical studies carried out in a very limited setting, such as hospitals or health centers. In all steps papers were reviewed and data extracted by two independent reviewers.

An exploratory analysis was performed taking into account the steps described below.

Articles retrieved were first sorted out by the following variables: language; target population (general or disease specific), year of publication; type of study (empiric or review); first authors' country of residence and affiliation; countries covered.

It was observed that a great part of papers retrieved covered Brazil and were produced by Brazilian authors. In order to avoid taking Brazilian production trends as the general one, data were stratified by countries covered (Brazil; LAC excluding Brazil; and multicountry studies) and first authors' country of residence (Brazil; LAC excluding Brazil; and EU / USA), when analyzing time trends.

Second, based on Hanson *et al* [17], papers were categorized by level of the health system addressed: I) patients, households and communities; II) health services delivery; III) health sector (policies or institutions); IV) national policies or institutions cutting across sectors; and V) regional and international policies and institutions.

Third, they were classified according to ATM domains [18] as follows: a) medicines selection and use (consumption, rational use); b) sustainable financing, affordability and price of medicines; c) leadership and governance (policies formulation and implementation,

legislation, health litigation); d) availability of medicines; e) human resources for health; f) quality of medicines and quality assurance systems'; g) medicines information and information systems.

Finally, based on articles' research questions, research issues were identified and categorized by consensus among authors in nineteen categories, such as medicines use, availability, financing model, affordability etc.

Results

A total of 77 scientific articles were retained after the selection process as depicted on Figure 1.

Around half of the retained papers (53.7%) were published in English, 37.7% in Portuguese and 9.1% in Spanish. Most of them (72.7%) targeted general populations. The majority of studies (85.7%) were empiric - quantitative and qualitative approaches were adopted in 58.4% and 22.1% respectively; mixed-methods were used in the remaining 19.5%.

Regarding first author's country of residence, Brazil was the leader (57.1%), followed by the United States of America (USA) (20.8%). First author's affiliation was linked to academic institutions in 76.6% of the papers.

The top five countries covered were Brazil (68.8%), Mexico (15.6%), Colombia (11.7%), Argentina (10.4%) and Peru (10.4%). This picture changes when studies covering a single country are considered, for instance, Brazil accounted for 55.8%, while the above mentioned countries accounted for 6.5%, 3.9%, 1.3% and 3.9%, respectively.

First authors of the seventeen multi-country studies (22.1% out of 77) were mostly affiliated to institutions from the USA (8) and Brazil (5).

Multi-country studies are mostly published in English (94.1%), as well as those addressing LAC (excluding Brazil) countries. For studies covering Brazil the preferential language was Portuguese (65.1%).

When the first author's country of origin was Brazil, Portuguese was the most frequent language of publication (65.9%). In LAC countries around a half of the publications are in Spanish (55.6%) and when first author's country of origin was in the EU or the USA, English was the language of all papers.

An increasing number of publications relating to ATM were found (Figure 2, A). The overall correlation (r) reflecting the association between the number of publications and year was 0.93 ($p=0.00$). The R^2 value 0.85 indicates a significant sustained increase over the 10 years. This increase refers mostly to publications addressing Brazil as study setting (r 0.89, $p<0.01$, R^2 0.79 – Figure 2, B) and less extensively to those addressing more than one country (r 0.69, $p<0.05$, R^2 0.48 – Figure 2, C). The slight increase in the number of publications on ATM addressing single LAC countries, excluding Brazil, however, shows little statistical significance (r 0.56, $p<0.10$, R^2 0.31 – Figure 2, D). The analysis by country of residence of the first author points out to similar trends, as can be observed on Figure 2, E: authors from Brazil responded for the higher growth rate (r 0.87, $p<0.01$, R^2 0.76), followed by those from high-income countries (r 0.78, $p<0.01$, R^2 0.61), and other LAC countries (r 0.59, $p<0.10$, R^2 0.34).

As Table 1 shows, ‘Health sector’, ‘Health services delivery’ and ‘Patients, household and communities’ were the three health system levels most frequently addressed. Regarding ATM Domains, ‘Leadership and governance’, ‘Sustainable financing, affordability and price of medicines’, ‘Medicines selection and use’ and ‘Availability of medicines’ were the top four explored.

‘Medicines Use’ (18.2%), ‘Availability’ (16.9%), ‘Medicines price/Affordability’ (14.3%), ‘Financing model of medicines’ and ‘Health Litigation’ (11.7%), ‘Policy implementation’ (11.7%) and Multisource medicines/Generics (10.4%) were the topmost research issues.

Discussion

The growth trend in the production of papers relating to access to medicines in LAC countries found in this study is consistent with the findings of other studies [12 13]. Nevertheless, rather than contributing to a steep increase in the number of papers in 2007, as referred by Ritz *et al.* [13], this study shows a consistent trend of growth in Brazil’s production from 2000 to 2010. As previously mentioned, this production accounts for most of the general growth identified in America’s LMIC.

Actually, an important and rapid growth of scientific production in Brazil has been observed in the last decade, especially in the field of public health [19].

There are at least two main reasons to explain this picture. First, there has been a longstanding investment in capacity building for research in Brazil since mid 1970s. Second, since 2003 Brazilian government, among other initiatives, has been increasing funds and grants for scientific research in priority areas of knowledge, which includes public health [20 21]. Moreover, only five countries in the region have health research agendas (Argentina, Brazil, Costa Rica, Paraguay and Peru) and only two of them (Brazil and Paraguay) explicitly include ATM issues [22].

The majority of papers published in Portuguese, in one hand, reflect scientific production leadership of Brazil in LAC and, on the other hand, the importance of the increasing public financing for research driven by Ministry of Health priorities. In this case, rather than focus on the dialogue with the international community of researchers, Brazilian authors gave priority to provide health authorities and national researchers with relevant information that can be used to promote improvements of the health system [19].

However, it is noteworthy that a trend in the growth of publications in English [23] was also observed, especially when multi-country studies were concerned. It reflects the interest of high-income countries' authors in the implementation of ATM policies in the sub-region. This also indicates an effort developed by LAC researchers in order to contribute to the discussion of internationally relevant issues.

The choice for research method should be based on the research question, which means both qualitative or/and quantitative methods could be used. As the size of the effect is usually the crucial estimation considered, quantitative methods, particularly randomized clinical trials, have been preferred for producing evidence, including for social and health policy [24 25]. This same pattern was observed in this study. However, the importance of qualitative approach has been increasingly recognized and used for health services and public health studies [26].

A smaller proportion of studies employing qualitative methods was found, which indicates the need for a better balance between quantitative and qualitative research, in order to reflect context specificities as well as to enhance policy learning [27 28]. The similar proportion of studies using mixed-methods may demonstrate the complexity of access to medicines issues, within the broader HPSR field, referred by Gilson *et al* 2011 [27] and Sheikh *et al* [28] as demanding for interdisciplinary developments and a wide spectrum of methodologies.

Independently of the approach, the quality of studies is the critical issue to be considered, in order for the results to appropriately inform decision making [25 29].

Considering the Health System Levels, the most important point of discussion is the scarcity and low variety of issues addressed within Levels IV (national policies or institutions cutting across sectors) and V (Regional and international policies and institutions). This reflects the lack of attention in research that is given to: (a) national issues beyond the health sector, such as medicines production and legislation and regulation, since the few publications found in level IV focused on litigation and court decisions; (b) international issues, such as ‘Global Policies’ and ‘Human Rights’ and ‘International Legislation’. The majority of the studies in Level V addressed intellectual property issues. This points to the importance of approaching access to medicines in broader national and international contexts.

‘Human resources for health’, ‘Quality of medicines and quality and quality assurance systems’, and ‘Medicines information and information systems’ are the domains that present a research gap. It is noteworthy that two of the most important health system building blocks [12], ‘Human resources’ and ‘Health information’, are missing publications in the ATM theme.

The categorization according to issues clearly shows concentration of publications in some, more traditional areas – ‘Medicines Use’, ‘Availability’, ‘Medicines price/Affordability’ and ‘Financing model of medicines’, directly related to the WHO ATM framework [10]. Meanwhile, there are research gaps in other important areas as ‘Human resources for health’, ‘Global policies and human rights’, ‘Production of medicines’ and ‘Traditional medicine’.

No judgment on quality criteria was applied to papers retrieved, so this aspect was not considered on the trends addressed. Despite a language criterion was used on initial search filters, only two countries in the region have different native languages from those included. Due to feasibility, open sources and the Brazilian academic public database – Periódicos CAPES – were used to recover full texts. However, this database is fairly broad (around 20,000 journals) and papers not available there or in open sources are hardly accessible to researchers or policymakers in the region. Therefore, this was not considered a relevant bias. Publications were assumed here as *proxys* of research production. Notwithstanding barriers as the acceptability of local approaches in high impact scientific journals, difficulties in scientific

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4 writing and writing in English [30] have a negative impact in the conversion of research
5 findings in scientific communications.
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8 Since “access to medicines” is not a Mesh term and the existing Mesh terms are not suitable, a
9 broad range of terms were used in order to get the best possible coverage of relevant papers.
10 Moreover by retaining only the available full text article , the results might be influenced by
11 the "full text bias".
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15 It was possible to identify relevant scientific publication trends on ATM reflecting a growing
16 research capacity in the region, but concentrated in few countries and research themes. This
17 apparent gap on research capacity in many LMIC could be overcome through research
18 collaboration among countries. Thus health research funders should promote this type of
19 arrangement, to enhance and take advantage of the existing capacity, while fostering a more
20 balanced development in the region. Also, a number of publications involving researchers and
21 institutions from high-income countries was identified. It is important to strengthen this
22 collaboration ensuring that interests and needs from the LMIC are addressed and local
23 capacity building is promoted.
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The authors do not identify any competing interest related to this study.

Box 1 – Search strategy for scientific publication on access to medicines in Latin America and Caribbean syntax by Database. 2000-2010

Database	Search Strategy syntax	Note
Medline	("pharmaceutical preparations"[MeSH Terms] OR "drugs, essential"[MeSH Terms] OR "drugs, generic"[MeSH Terms]) AND ("health services accessibility"[MeSH Terms] OR "health policy"[MeSH Terms]) AND ("humans"[MeSH Terms] AND (English[lang] OR Spanish[lang] OR Portuguese[lang])) AND ("2000/01/01"[PDAT] : "2010/09/30"[PDAT])) AND ("humans"[MeSH Terms] AND (English[lang] OR Spanish[lang] OR Portuguese[lang])) AND ("2000/01/01"[PDAT] : "2010/09/30"[PDAT]))	Thesaurus exists These terms were identified with the support of an expert on bibliography search strategy.
Lilacs	<p>Portuguese ((Preparações Farmacêuticas) OR (Medicamentos Essenciais) OR (Medicamentos Genéricos)) AND ((Acesso aos serviços de saúde) OR (Política de Saúde)) em assunto (search for Mesh/Desc terms)</p> <p>Spanish ((Preparaciones Farmacéuticas) OR (Medicamentos Essenciales) OR (Medicamentos Genéricos)) AND ((Accesibilidad de los Servicios de Salud) OR (Política de Salud))</p> <p>English ((Pharmaceutical Preparations) OR (Drugs, Essential) OR (Drugs, Generic)) AND ((Health Services Accessibility) OR (Health Policy))</p>	
Scopus	(TITLE-ABS-KEY("access to medicines" OR "Medicines Price" OR "Rational use of medicine" OR "medicines affordability" OR "affordability of medicines" OR "accessibility of medicines" OR "medicines accessibility" OR "Medicines financing" OR "Availability of medicines" OR "medicines availability") AND SUBJAREA(mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal OR mult OR arts OR busi OR deci OR econ OR psyc OR soci) AND PUBYEAR AFT 1999 AND PUBYEAR BEF 2011)	Thesaurus does not exist These terms came from the guiding template proposed by ARPHSP and agreed in the Siem Reap Meeting (WHO, 2010 #2439).
ISI	Topic=(access to medicines OR "Medicines Price" OR "Rational use of medicines" OR "medicines affordability" OR "affordability of medicines" OR "accessibility of medicines" OR "medicines accessibility" OR "Medicines financing" OR "Availability of medicines" OR "medicines availability") Refined by: Languages=(ENGLISH OR PORTUGUESE OR SPANISH) AND Publication Years=(2010 OR 2003 OR 2009 OR 2004 OR 2008 OR 2001 OR 2007 OR 2000 OR 2006 OR 2005)	

Figure 1. Stepwise process for selection of papers concerning access to medicines in Latin America and Caribbean. 2000-2010.

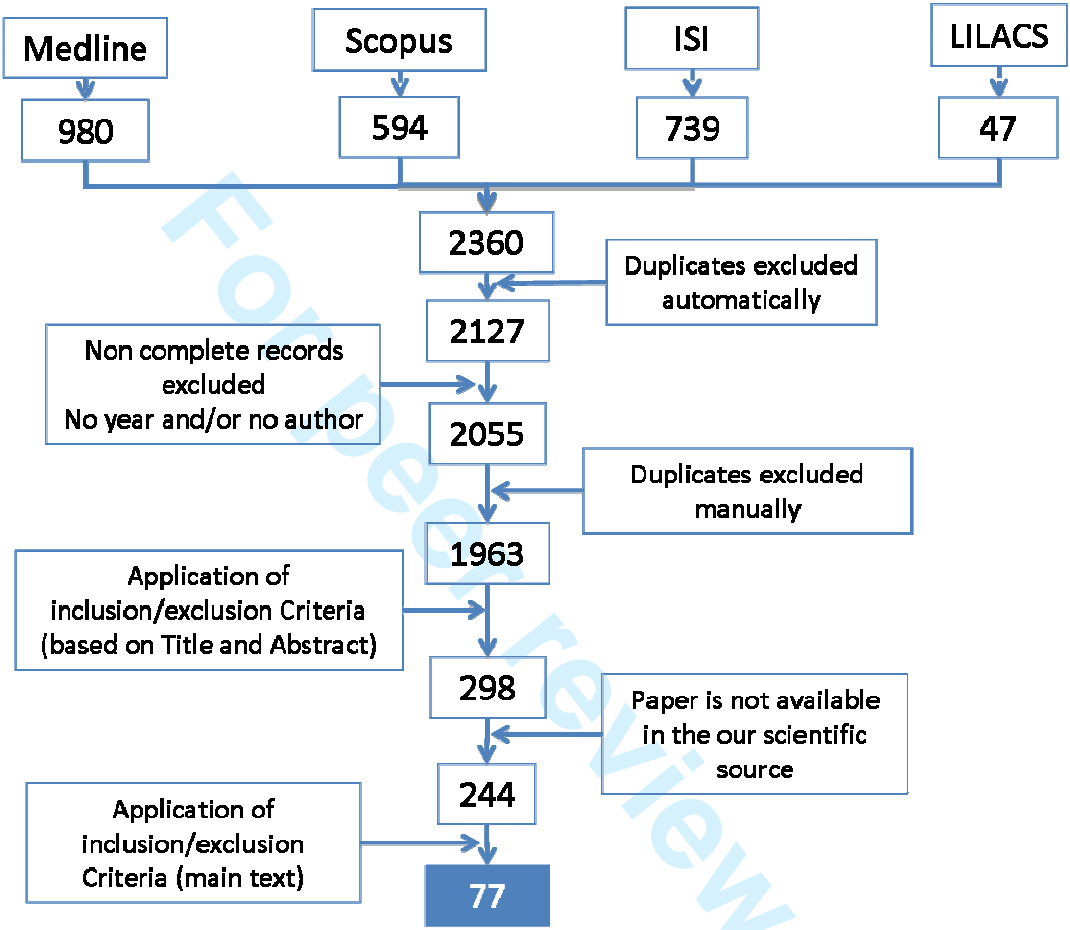


Figure 2. Number of papers related to access to medicines in Latin America and Caribbean per year by country covered and country of the corresponding author, 2000 – 2010.

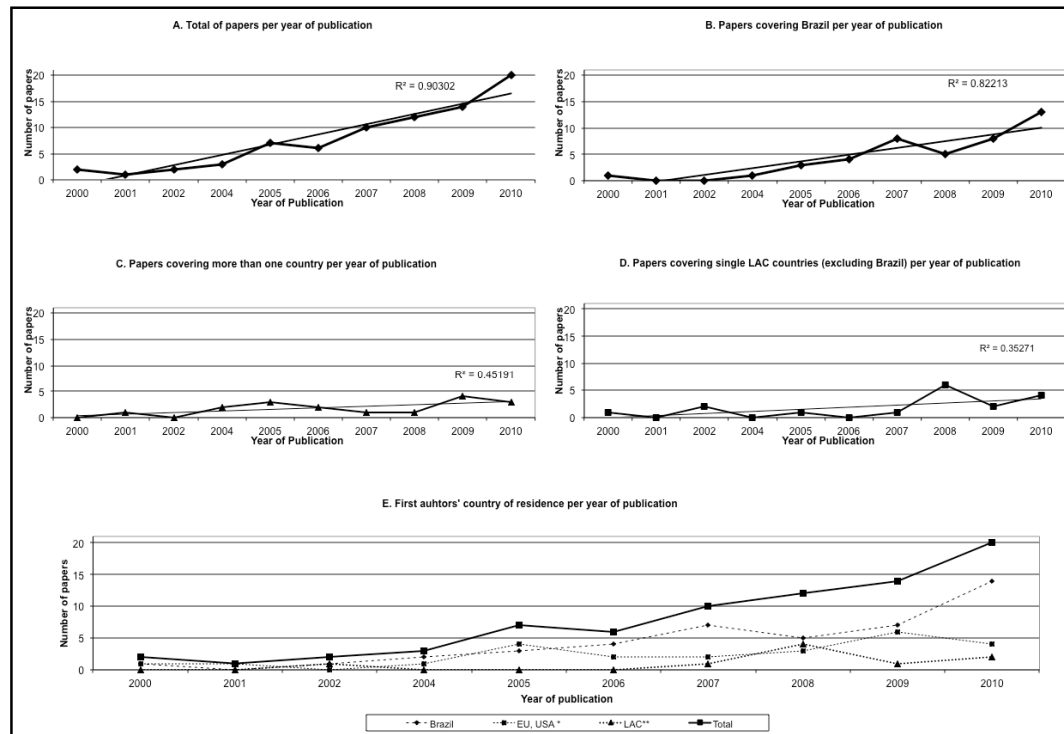


Table 1. Distribution of papers by Health System Level, Access to Medicine Domain and Research issue. 2000-2010.

Classification/Categories	Frequency (N)	Percent* (%)
<i>Health System Levels</i>		
Health sector (policies or institutions)	41	35.34%
Health services delivery	30	25.86%
Patients, households and communities	28	24.14%
National policies or institutions cutting across sectors	11	9.48%
Regional and international policies and institutions	6	5.17%
<i>Domains</i>		
Leadership and governance	25	26.04%
Sustainable financing and affordability and price of medicines	22	22.92%
Medicines selection and use	21	21.88%
Availability of medicines	16	16.67%
Human resources for health	3	3.13%
Quality of medicines and quality and quality assurance systems	3	3.13%
Medicines information and information systems	2	2.08%
N/A	4	4.17%
<i>Research issue</i>		
Medicines Use	14	18.20%
Availability	13	16.90%
Medicines price/Affordability	11	14.30%
Financing model of medicines	10	13.00%
Health Litigation	9	11.70%
Policy implementation	9	11.70%
Multisource medicines/ Generics	8	10.40%
Legislation and regulation	5	6.50%
Good Pharmacy Practices	4	5.20%
IP related issues	4	5.20%
Evidence and health policy	3	3.90%
Methods	3	3.90%
Socioeconomic Determinants	3	3.90%
Health care and medicines seeking behavior	2	2.60%
Provision model of medicines	2	2.60%
Human resources for health	1	1.30%
Global policies and human rights	1	1.30%
Production of medicines	1	1.30%
Traditional medicine	1	1.30%

Categories are not mutually exclusive

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CONTRIBUTORSHIP STATEMENT

Isabel Cristina Martins Emmerick, ScD, MSc – conception of the paper, outlined the first draft, performed statistical analysis, participated in writing and reviewing the text and approved the submitted version.

Maria Auxiliadora Oliveira, ScD, M.D., MSc - conception of the paper, outlined the first draft, participated in writing and reviewing the text and approved the submitted version.

Vera Lucia Luiza, ScD, MSc - coordinated the general project from where the approach belongs to, participated in the conception of the paper, participated in writing and reviewing the text and approved the submitted version.

Thiago Botelho Azeredo, ScD, MSc - contributed with statistical analysis, participated in writing and reviewing the text and approved the submitted version.

Maryam Bigdeli, PharmD, MPH - contributed in the discussion section, participated in reviewing the text and approved the submitted version.

COMPETING INTERESTS

None

DATA SHARING

The complete database of retrieved papers and all the search history is available with corresponding author and also with the funder.

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Priority policy issue	Total of papers	%
Medicines Use	14	18%
Availability	13	17%
Financing model of medicines	10	13%
Lawsuit	9	12%
Policies	9	12%
Generics	8	10%
Medicines price	7	9%
Legislation and regulation	5	6%
Affordability	4	5%
Good Pharmacy Practices	4	5%
Evidence and health policy	3	4%
IP	3	4%
Methods	3	4%
Socioeconomic Determinants	3	4%
Provision model of medicines	2	3%
Cross border consumption	1	1%
Health care seeking behavior	1	1%
Human resources for health	1	1%
Global pol policies and human rights	1	1%
Production of medicines	1	1%
Regional trade agreement	1	1%
Traditional medicine	1	1%
	104	

	Priority policy issue
Medicines Use	Medicines Use
Availability	Availability
Financing model of medicines	Medicines price/Affordability
Lawsuit	Financing model of medicines
Policies	Lawsuit
Generics	Policies
Medicines Prices/Affordability	Generics
Legislation and regulation	Legislation and regulation
go to Medicines Prices	Good Pharmacy Practices
Good Pharmacy Practices	IP related issues
Evidence and health policy	Evidence and health policy
IP	Methods
Methods	Socioeconomic Determinants
Socioeconomic Determinants	Health care and medicines seeking behavior
Provision model of medicines	Provision model of medicines
go to Health care and medicines seeking behavior	Human resources for health
Health care and medicines seeking behavior	Global pol policies and human rights
Human resources for health	Production of medicines
Global pol policies and human rights	Traditional medicine
Production of medicines	The categories are not mutual excludent, the perc
go to IP related	
Traditional medicine	

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Total	%
14	18.2%
13	16.9%
11	14.3%
10	13.0%
9	11.7%
9	11.7%
8	10.4%
5	6.5%
4	5.2%
4	5.2%
3	3.9%
3	3.9%
3	3.9%
2	2.6%
2	2.6%
1	1.3%
1	1.3%
1	1.3%
1	1.3%
Percentage does not sum 100%	

<i>Health System Levels</i>	<i>Frequency (N)</i>	<i>Percent* (%)</i>
Health sector (policies or institutions)	41	35.34%
Health services delivery	30	25.86%
Patients, households and communities	28	24.14%
National policies or institutions cutting across sectors	11	9.48%
Regional and international policies and institutions	6	5.17%

*The categories are not mutual excluding, the percentage does not sum 100%

<i>Domains</i>	<i>Frequency (N)</i>	<i>Percent* (%)</i>
Medicines selection and use (consumption, rational use)	21	21.88%
Sustainable financing and affordability and price of medicines	22	22.92%
Leadership and governance	25	26.04%
Availability of medicines	16	16.67%
Human resources for health	3	3.13%
Quality of medicines and quality and quality assurance systems	3	3.13%
Medicines information and information systems	2	2.08%
N/A	4	4.17%

*The categories are not mutual excluding, the percentage does not sum 100%

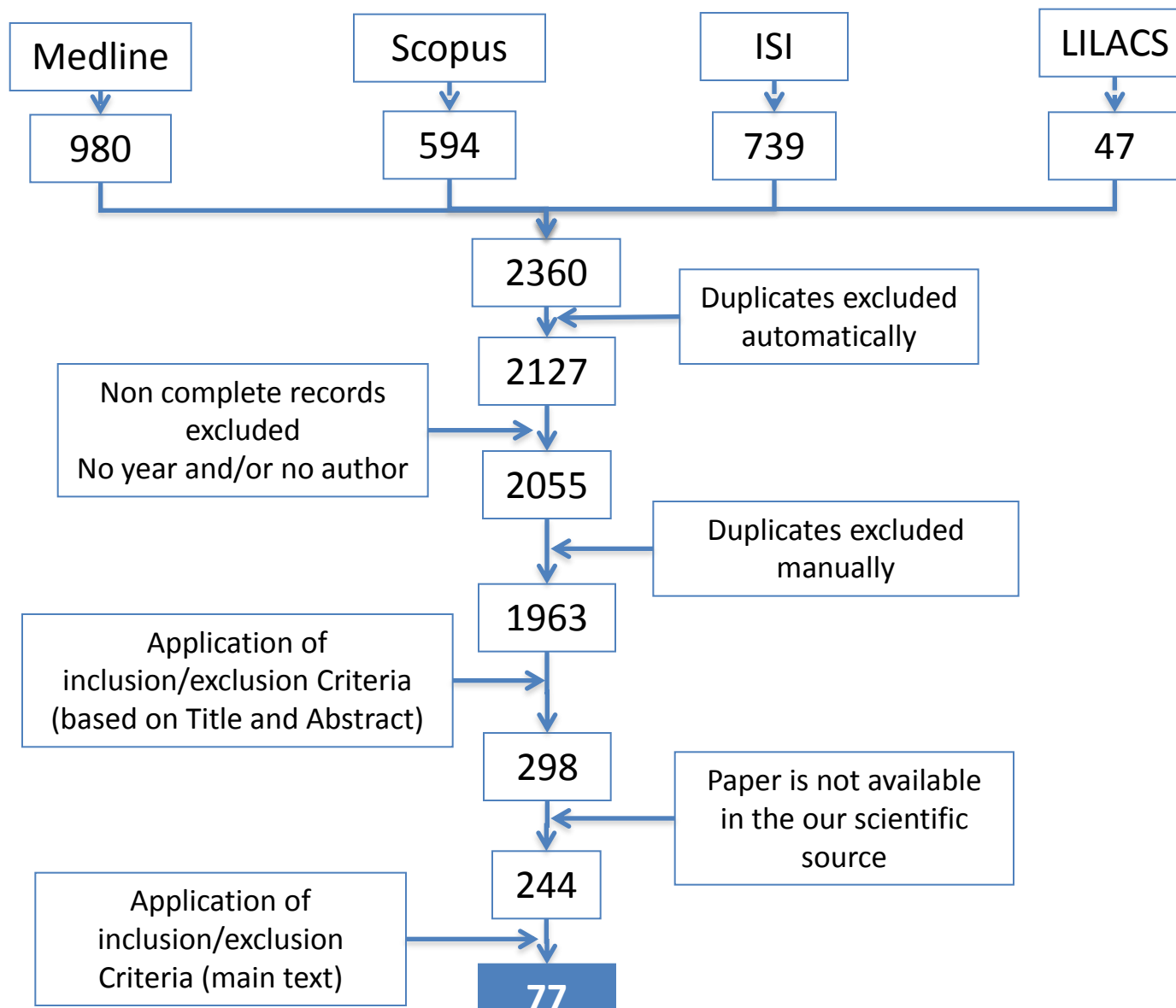
<i>Priority research issue</i>	<i>Frequency (N)</i>	<i>Percent* (%)</i>
Medicines Use	14	18.20%
Availability	13	16.90%
Medicines price/Affordability	11	14.30%
Financing model of medicines	10	13.00%
Health Litigation	9	11.70%
Policy implementation	9	11.70%
Multisource medicines	8	10.40%
Legislation and regulation	5	6.50%
Good Pharmacy Practices	4	5.20%
IP related issues	4	5.20%
Evidence and health policy	3	3.90%
Methods	3	3.90%
Socioeconomic Determinants	3	3.90%
Health care and medicines seeking behavior	2	2.60%
Provision model of medicines	2	2.60%
Human resources for health	1	1.30%
Global policies and human rights	1	1.30%
Production of medicines	1	1.30%
Traditional medicine	1	1.30%

The categories are not mutual excluding, the percentage does not sum 100%

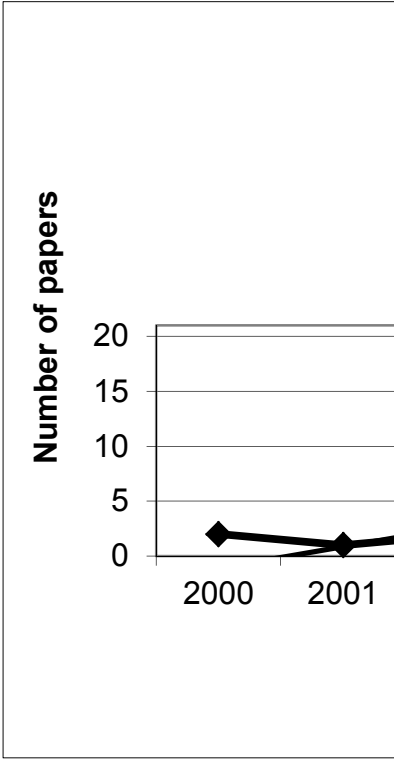
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For peer review only

Figure 1. Stepwise process for selection of papers concerning access to medicines in Latin America and Caribbean. 2000-2010



		Year of Publication			
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	2000	2	2.6	2.6	2.6
	2001	1	1.3	1.3	3.9
	2002	2	2.6	2.6	6.5
	2004	3	3.9	3.9	10.4
	2005	7	9.1	9.1	19.5
	2006	6	7.8	7.8	27.3
	2007	10	13.0	13.0	40.3
	2008	12	15.6	15.6	55.8
	2009	14	18.2	18.2	74.0
	2010	20	26.0	26.0	100.0
	Total	77	100.0	100.0	



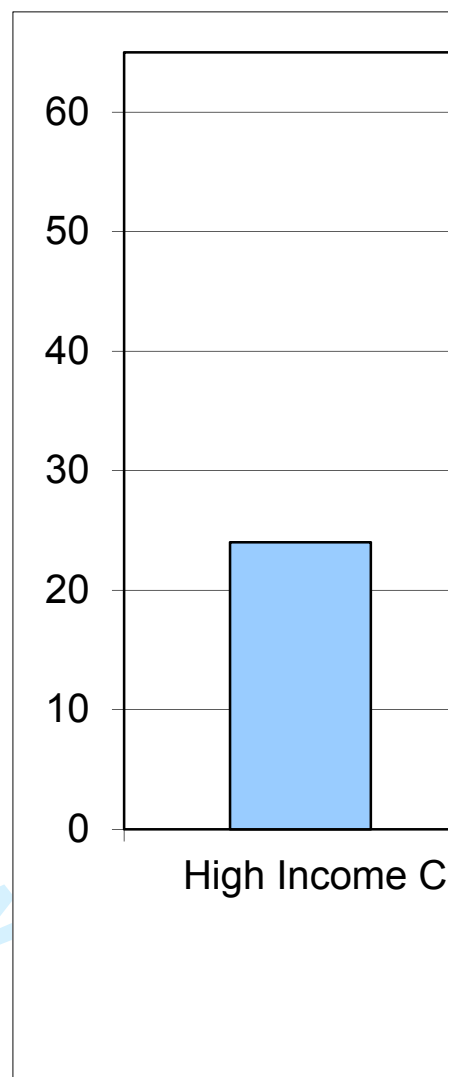
R2= 0,903

World bank Class author

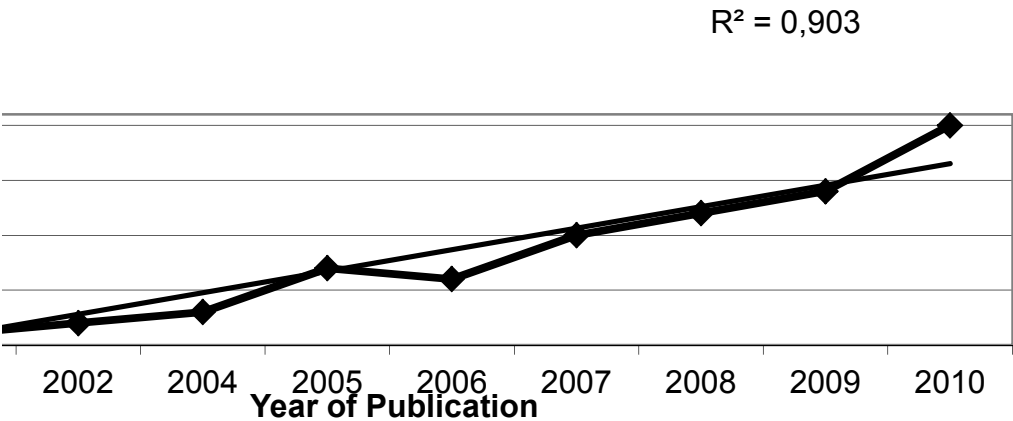
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	High Income Country	24	31.2	31.2	31.2
	Upper Middle Income Country	52	67.5	67.5	98.7
	Low Middle Income Country	1	1.3	1.3	100.0
	Total	77	100.0	100.0	

World bank Class country

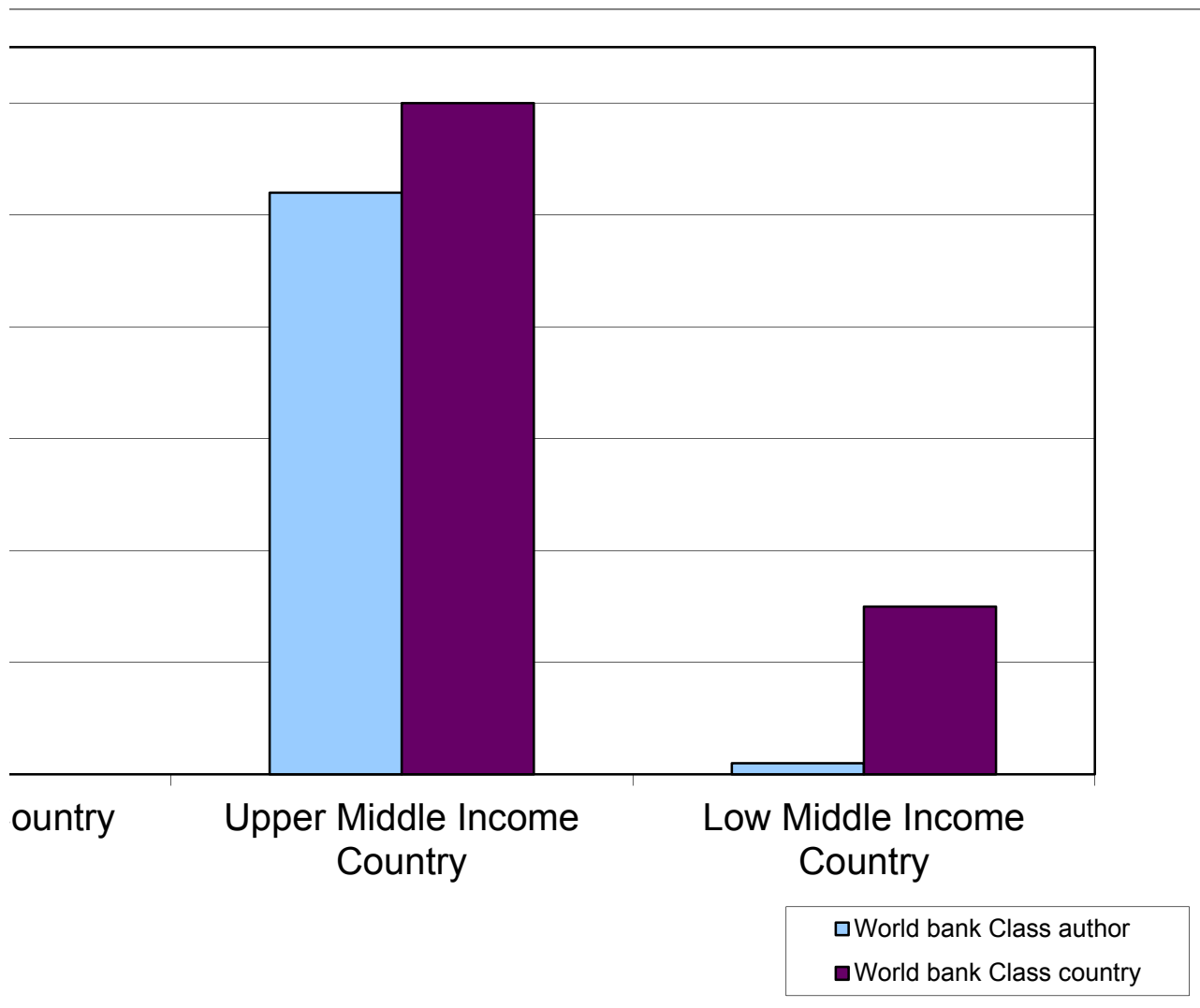
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	High Income Country				
	Upper Middle Income Country	60	77.9	80.0	80.0
	Low Middle Income Country	15	19.5	20.0	100.0
	Total	75	97.4	100.0	
Missing	System	2	2.6		
Total		77	100.0		



A. Total of papers per year of publication



review only





Access to Medicines in Latin America and the Caribbean (LAC): a scoping study

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Manuscript ID:	bmjopen-2012-002224.R1
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Primary Subject Heading:	Evidence based practice
Secondary Subject Heading:	Health policy, Research methods, Global health, Pharmacology and therapeutics, Health economics
Keywords:	Health policy < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, PUBLIC HEALTH, SYSTEMATIC REVIEWS

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Manuscripts

Access to Medicines in Latin America and the Caribbean (LAC): a scoping study

Running title: Scoping study on access to medicines

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Keywords: Access to medicines; Bibliometrics; Low and middle-income countries; Latin America; Caribbean region

Word count: 2476 words and 14174 characters (no space)

Abstract

Objective: To assess scientific publication trends on Access to Medicines (ATM) in Latin America and the Caribbean (LAC) low and middle income countries (LMIC) and to map research gaps, focusing on methodological approaches used to study ATM, institutions and countries involved as well as the main issues raised by authors.

Search strategy: A scoping study of the scientific literature on ATM was performed, on Medline, ISI, SCOPUS and Lilacs databases from 2000 to 2010.

Selection criteria: Research articles and reviews published in English, Spanish and Portuguese were included. Studies including only high-income countries were excluded, as well as those carried out in very limited settings and discussion papers.

Data extraction: The 77 articles retained were categorized through consensus among the research team according to the level of the health system addressed, ATM domain and research issues covered.

Results: Publications on ATM have increased over time during the study period ($r = 0.93$, $p = 0.00$; $R^2 = 0.85$). The top five countries covered were Brazil (68.8%), Mexico (15.6%), Colombia (11.7%), Argentina (10.4%) and Peru (10.4%). 'Health services delivery' and 'Patients, household and communities' were the health system levels most frequently covered. The ATM Domains 'Leadership and governance', 'Sustainable financing, affordability and price of medicines', 'Medicines selection and use' and 'Availability of medicines' were the top four explored. There are research gaps in important areas, such as 'Human resources for health', 'Global policies and human rights', 'Production of medicines' and 'Traditional medicine'.

Conclusions: The upward trend on scientific publication reflects a growing research capacity in the region, which is concentrated on research teams in selected countries. The gaps on research capacity could be overcome through research collaboration among countries. It is important to strengthen these collaborations, assuring that interests and needs from the LMIC are addressed and local capacity building is promoted.

Key words Access to medicines; Bibliometrics; Scoping study; Low and middle-income countries; Latin America; Caribbean region.

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ARTICLE SUMMARY

Article focus

- To identify methodological approaches and research issues which address access to medicines (ATM) in Latin American and the Caribbean (LAC) in the published literature.
- To learn about LAC researchers’ capacity to produce evidence on ATM through articles published in peer-reviewed journals.
- To identify research gaps on ATM that should be addressed in future studies.
- To map potential opportunities for south-south collaboration on ATM research.

Key messages

- An increasing trend in scientific publications on ATM reflects a growing research capacity in LAC.
- Scientific publications in peer-reviewed journals are concentrated in few countries and focus on well-established areas and themes.
- ‘Health services delivery’ and ‘Patients, household and communities’ were the health system levels most frequently covered.
- The ATM Domains, ‘Leadership and governance’, ‘Sustainable financing, affordability and price of medicines’, ‘Medicines selection and use’ and ‘Availability of medicines’ were the top four explored.

Strengths and Limitations

- Local databases in Spanish and in Portuguese, the main languages in the region, which are generally not covered in other similar studies, were searched.
- A quality assessment of the papers retained was performed.

Introduction

Access to medicines (ATM) is a key component of health care systems. The provision of regular access to affordable, appropriate and high-quality medicines has been established as a global priority, highlighted in several international commitments such as World Health Assembly's resolutions [1-4], Millennium Development Goals [5], UNGASS declarations [6 7], the Oslo Declaration [8] and the Political Declaration on HIV and AIDS: Intensifying Our Efforts to Eliminate HIV and AIDS [9]. In line with these commitments, governments of many Low and Middle Income Countries (LMIC) have implemented policies aimed at improving ATM.

Scaling-up ATM in low- and middle-income countries (LMIC) has been a major challenge faced by governments and health authorities. The delivery of medicines to most people in need depends on a series of efforts related to different access components or dimensions such as, sustainable financing, the existence of a network of reliable health services, and an efficient supply chain management [10].

In this context, the existence of reliable and accurate information on the different components of ATM is crucial for better decision-making. Despite the growing number of studies on issues like price and availability [11], quality data on access to and use of medicines are still lacking [12 13].

This work is part of activities carried out within the ATM policy research program, recently implemented by the Alliance for Health Policy and System Research (AHPSR) [14].

This paper aims to assess scientific publication trends on ATM in Latin America and the Caribbean (LAC) and to map research gaps.

Methods

A scoping study [15 16] of the scientific literature on ATM was performed covering ten years, from January 2000 to September 2010. This review intended to map scientific production on ATM related topics in LAC focusing on methodological approaches used to study ATM, institutions and countries involved as well as the main issues raised by authors.

Databases searched were Medline, ISI, SCOPUS and Lilacs, covering publications on ATM in the in the fields of health, social sciences and humanities. Search terms were set and combined according to the database features (Box 1).

The articles identified were screened and selected according to inclusion criteria, as follows: focus on ATM; addressing at least one LMIC at national or sub-national levels (districts, provinces, states); written in English, Spanish and Portuguese languages; abstract available; full-text available in open-access journals and on *Periódicos CAPES* e-journals database. Both and empiric and reviews articles were included. For review articles, some additional inclusion criteria applied: the article must include information on how the literature search was done and which scientifically recognized index was used; selection criteria must define the type of articles included in the review. Exclusion criteria were: studies including only high-income countries; empirical studies carried out in a very limited setting, such as hospitals or health centers. In all steps papers were reviewed and data extracted by two independent reviewers.

An exploratory analysis was performed taking into account the steps described below.

Articles retrieved were first sorted out according to the following variables: language; target population (general or disease specific), year of publication; type of study (empiric or review); first authors' country of residence and affiliation; countries covered.

Second, based on Bigdeli et al. [17], papers were categorized by level of the health system addressed: I) patients, households and communities; II) health services delivery; III) health sector (policies or institutions); IV) national policies or institutions cutting across sectors; and V) regional and international policies and institutions.

Third, they were classified according to ATM domains [18] as follows: a) medicines selection and use (consumption, rational use); b) sustainable financing, affordability and price of medicines; c) leadership and governance (policies formulation and implementation, legislation, health litigation); d) availability of medicines; e) human resources for health; f) quality of medicines and quality assurance systems'; g) medicines information and information systems.

Fourth, based on articles' research questions, research issues were identified and categorized by consensus among authors in nineteen categories related to each of the above ATM domains (Box 2)

Descriptive statistics (frequencies and percentages) were calculated to characterize distribution of papers according to the variables and categories mentioned above. Linear regression was performed to test the relationship between number of papers and year of publication. The strength and direction of this association was estimated by calculating the correlation coefficient (Pearson's r) and its statistical significance (p-value). Data linearity fit was expressed by coefficient of determination (R^2). Identified trends were depicted on scatter plots.

It was observed that a great part of papers retrieved covered Brazil and were produced by Brazilian authors. In order to avoid taking Brazilian production trends as the general one, data were stratified by countries covered (Brazil; LAC excluding Brazil; and multi-country studies) and first authors' country of residence (Brazil; LAC excluding Brazil; and EU / USA), when analyzing time trends.

Results

A total of 77 scientific articles were retained after the selection process as depicted in Figure 1.

Around half of the retained papers (53.7%) were published in English, 37.7% in Portuguese and 9.1% in Spanish. Most of them (72.7%) targeted general population. The majority of studies (85.7%) were empiric - quantitative and qualitative approaches were adopted in 58.4% and 22.1% respectively; mixed-methods were used in the remaining 19.5%.

Regarding first author's country of residence, Brazil was the leader (57.1%), followed by the United States of America (USA) (20.8%). First author's affiliation was linked to academic institutions in 76.6% of the papers.

The top five countries covered were Brazil (68.8%), Mexico (15.6%), Colombia (11.7%), Argentina (10.4%) and Peru (10.4%). This picture changes when multi-country studies are excluded and only studies covering a single country are considered: in such case, Brazil accounted for 55.8% of publications, while the above mentioned countries accounted for 6.5%, 3.9%, 1.3% and 3.9%, respectively.

First authors of the seventeen multi-country studies (22.1% out of 77) were mostly affiliated to institutions from the USA (8) and Brazil (5).

Multi-country studies were mostly published in English (94.1%), especially those covering LAC excluding Brazil. For studies covering Brazil the preferential language was Portuguese (65.1%).

When the first author’s country of residence was Brazil, Portuguese was the most frequent language of publication (65.9%). In LAC countries, excluding Brazil, around half of the publications were in Spanish (55.6%) and when first author’s country of residence was in the EU or the USA, English was the language of publication for all papers.

The number of publications related to ATM increased over time during the study period (Figure 2, A). The overall correlation (r) reflecting the association between the number of publications and year was 0.93 (p=0.00). The R² value 0.85 indicates a significant sustained increase over the 10 years covered by the study period. This increase refers mostly to publications covering Brazil as study setting (r 0.89, p<0.01, R² 0.79 – Figure 2, B) and less extensively to those covering more than one country (r 0.69, p<0.05, R² 0.48 – Figure 2C). The slight increase in the number of publications on ATM covering single LAC countries, excluding Brazil, however, shows little statistical significance (r 0.56, p<0.10, R² 0.31 – Figure 2, D). The analysis by country of residence of the first author points out to similar trends, as can be observed in Figure 2E: publication with authors from Brazil responded for the higher growth rate (r 0.87, p<0.01, R² 0.76), followed by those from high-income countries (r 0.78, p<0.01, R² 0.61), and other LAC countries (r 0.59, p<0.10, R² 0.34).

As Table 1 shows, ‘Health sector’, ‘Health services delivery’ and ‘Patients, household and communities’ were the three health system levels most frequently covered. The ATM Domains ‘Leadership and governance’, ‘Sustainable financing, affordability and price of medicines’, ‘Medicines selection and use’ and ‘Availability of medicines’ were the top four explored.

The top most researched issues were ‘Medicines Use’ (18.2%), ‘Availability’ (16.9%), ‘Medicines price/Affordability’ (14.3%), ‘Financing model of medicines’ and ‘Health Litigation’ (11.7%), ‘Policy implementation’ (11.7%) and Multisource medicines/Generics (10.4%).

Discussion

The growing trend in the production of papers related to ATM in LAC countries found in this study is consistent with the findings of other studies [12 13]. However Ritz *et al.* [13] report a steep increase in the number of papers in 2007, while this study shows a consistent trend of growth in Brazil's production from 2000 to 2010. As previously mentioned, this production accounts for most of the general growth identified in America's LMIC. This is consistent with an important and rapid growth of general scientific production in Brazil which been observed in the last decade, especially in the field of public health [19].

There are at least two main reasons to explain this picture. First, there has been a longstanding investment in capacity building for research in Brazil since mid 1970s. Second, since 2003 Brazilian government, among other initiatives, has been increasing funds and grants for scientific research in priority areas of knowledge, which includes public health [20 21]. Moreover, only five countries in the region have official health research priority agendas (Argentina, Brazil, Costa Rica, Paraguay and Peru) and only two of them (Brazil and Paraguay) explicitly include ATM issues [22].

The majority of papers published in Portuguese reflect the leadership of Brazil in the scientific production of LAC. This is also a consequence of the increasing public financing for research driven by Ministry of Health priorities. In this case, rather than focus on the dialogue with the international community of researchers, Brazilian authors gave priority to provide health authorities and national researchers with relevant information that can be used to promote improvements of the health system [19].

However, it is noteworthy that a trend in the growth of publications in English [23] was also observed, especially when multi-country studies were concerned. It reflects the interest of high-income countries' authors in the implementation of ATM policies in the sub-region. This also indicates an effort developed by LAC researchers in order to contribute to the discussion of internationally relevant issues, which takes place mainly in English language peer-reviewed journals.

The choice for research method should be based on the research question and both qualitative and/or quantitative methods are acceptable. However, as the size of the effect is usually a crucial estimation, quantitative methods, particularly randomized clinical trials, have been preferred for producing evidence, including for social and health policy [24 25]. More

recently, the importance of qualitative approach has been increasingly recognized and used for health services and public health studies [26] This same pattern was observed in our study.

A smaller proportion of studies employing qualitative methods was found, which indicates the need for a better balance between quantitative and qualitative research, in order to reflect context specificities as well as to enhance policy learning [27 28]. The proportion of studies using mixed-methods may demonstrate the complexity of ATM issues, within the broader HPSR field, referred by Gilson *et al* 2011 [27] and Sheikh *et al* [28] who demand for interdisciplinary developments and a wide spectrum of methodologies.

Considering the Health System Levels, the most important point of discussion is the scarcity and small variety of issues addressed within Levels IV (national policies or institutions cutting across sectors) and V (Regional and international policies and institutions). This reflects the lack of attention in research that is given to: (a) national issues beyond the health sector and related to economy or trade, such as medicines production and legislation and regulation and (b) international issues, such as ‘Global Policies’ and ‘Human Rights’ and ‘International Legislation’. The few publications found in level IV focused on litigation and court decisions while. the studies in Level V addressed intellectual property issues. These findings point to the importance of approaching ATM in broader national and international contexts.

Research gaps were identified in the domains of ‘Human resources for health’, ‘Quality of medicines and quality and quality assurance systems’, and ‘Medicines information and information systems’. It is noteworthy that two of the most important health system building blocks [12], ‘Human resources’ and ‘Health information’, are under-represented in ATM research.

The categorization according to issues clearly shows concentration of publications in some, more traditional areas – ‘Medicines Use’, ‘Availability’, ‘Medicines price/Affordability’ and ‘Financing model of medicines’, directly related to the WHO ATM framework [10]. Meanwhile, there are research gaps in other important areas as ‘Human resources for health’, ‘Global policies and human rights’, ‘Production of medicines’ and ‘Traditional medicine’.

Our study presents several limitations. Independently of the approach, the quality of studies is a critical issue to be considered, in order for the results to appropriately inform decision making [25 29]. However, as we aimed at a comprehensive scoping study rather than an in-

depth literature review no judgment on quality criteria was applied to papers retrieved and this aspect was not considered in the trends addressed.

Regarding the language criterion, which was used on initial search filters, it should be noted that only two countries in the region have different native languages from those included. This filter was therefore not considered as a significant bias.

Due to feasibility, open sources and the Brazilian academic public database – *Periódicos CAPES* – were used to recover full texts. This database is fairly broad (around 20,000 journals) and papers not available there or through other open sources are hardly accessible to researchers or policymakers in the region. Therefore, this was not considered a relevant bias in terms of availability of evidence to guide further research and decision-making. Publications were assumed here as *proxys* of research production. However, barriers such as the acceptability of local approaches in high impact scientific journals, difficulties in scientific writing and writing in English [30] have a negative impact on the conversion of research findings in scientific communications.

Since “access to medicines” is not a Mesh term and the existing Mesh terms are not suitable, a broad range of terms were used in order to get the best possible coverage of relevant papers. Moreover by retaining only the available full text article, the results might be influenced by the “full text bias”.

Finally, despite the fact that the study covered a large period of 10 years, the search was limited to late 2010 and does not account for papers published in 2011 and 2012. This is a relative limitation as trends over time are analyzed and reveal significant changes over the past decade.

In conclusion, our study identified relevant scientific publication trends on ATM reflecting a growing research capacity in the region, but concentrated in few countries and research themes. This apparent gap on research capacity in many LMIC could be overcome through research collaboration among countries. Thus health research funders should promote this type of arrangement, to enhance and take advantage of the existing capacity, while fostering a more balanced development in the region. Also, a number of publications involving researchers and institutions from high-income countries was identified. It is important to strengthen this collaboration ensuring that interests and needs from the LMIC are addressed and local capacity building is promoted.

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The authors do not identify any competing interest related to this study.

Contributorship

Isabel Cristina Martins Emmerick, ScD, MSc – conception of the paper, outlined the first draft, performed statistical analysis, participated in writing and reviewing the text and approved the submitted version.

Maria Auxiliadora Oliveira, ScD, M.D., MSc - conception of the paper, outlined the first draft, participated in writing and reviewing the text and approved the submitted version.

Vera Lucia Luiza, ScD, MSc - coordinated the general project from where the approach belongs to, participated in the conception of the paper, participated in writing and reviewing the text and approved the submitted version.

Thiago Botelho Azeredo, ScD, MSc - contributed with statistical analysis, participated in writing and reviewing the text and approved the submitted version.

Maryam Bigdeli, PharmD, MPH - contributed in the discussion section, participated in reviewing the text and approved the submitted version.

Data Sharing

The complete database of retrieved papers and all the search history is available with corresponding author and also with the funder.

Funding

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Box 1 – Search strategy for scientific publication on access to medicines in Latin America and Caribbean syntax by Database. 2000-2010

Database	Search Strategy syntax	Note
Medline	("pharmaceutical preparations"[MeSH Terms] OR "drugs, essential"[MeSH Terms] OR "drugs, generic"[MeSH Terms]) AND ("health services accessibility"[MeSH Terms] OR "health policy"[MeSH Terms]) AND ("humans"[MeSH Terms] AND (English[lang] OR Spanish[lang] OR Portuguese[lang])) AND ("2000/01/01"[PDAT] : "2010/09/30"[PDAT])) AND ("humans"[MeSH Terms] AND (English[lang] OR Spanish[lang] OR Portuguese[lang])) AND ("2000/01/01"[PDAT] : "2010/09/30"[PDAT]))	Thesaurus exists These terms were identified with the support of an expert on bibliography search strategy.
Lilacs	<p>Portuguese ((Preparações Farmacêuticas) OR (Medicamentos Essenciais) OR (Medicamentos Genéricos)) AND ((Acesso aos serviços de saúde) OR (Política de Saúde)) em assunto (search for Mesh/Desc terms)</p> <p>Spanish ((Preparaciones Farmacéuticas) OR (Medicamentos Esenciales) OR (Medicamentos Genéricos)) AND ((Accesibilidad de los Servicios de Salud) OR (Política de Salud))</p> <p>English ((Pharmaceutical Preparations) OR (Drugs, Essential) OR (Drugs, Generic)) AND ((Health Services Accessibility) OR (Health Policy))</p>	
Scopus	(TITLE-ABS-KEY("access to medicines" OR "Medicines Price" OR "Rational use of medicine" OR "medicines affordability" OR "affordability of medicines" OR "accessibility of medicines" OR "medicines accessibility" OR "Medicines financing" OR "Availability of medicines" OR "medicines availability") AND SUBJAREA(mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal OR mult OR arts OR busi OR deci OR econ OR psyc OR soci) AND PUBYEAR AFT 1999 AND PUBYEAR BEF 2011)	Thesaurus does not exist These terms came from the guiding template proposed by AHPSR, 2012. [18]
ISI	Topic=(access to medicines OR "Medicines Price" OR "Rational use of medicines" OR "medicines affordability" OR "affordability of medicines" OR "accessibility of medicines" OR "medicines accessibility" OR "Medicines financing" OR "Availability of medicines" OR "medicines availability") Refined by: Languages=(ENGLISH OR PORTUGUESE OR SPANISH) AND Publication Years=(2010 OR 2003 OR 2009 OR 2004 OR 2008 OR 2001 OR 2007 OR 2000 OR 2006 OR 2005)	

Box 2 –Categories related to ATM domains

Categories
Medicines Use
Availability
Medicines price/Affordability
Financing model of medicines
Health Litigation
Policy implementation
Multisource medicines/ Generics
Legislation and regulation
Good Pharmacy Practices
IP related issues
Evidence and health policy
Methods
Socioeconomic Determinants
Health care and medicines seeking behavior
Provision model of medicines
Human resources for health
Global policies and human rights
Production of medicines
Traditional medicine

FIGURE LEGENDS

Figure 1. Stepwise process for selection of papers concerning access to medicines in Latin America and Caribbean. 2000-2010.

Figure 2. Number of papers related to access to medicines in Latin America and Caribbean per year by country covered and first author's country of residence, 2000 – 2010.

For peer review only

Table 1. Distribution of papers by Health System Level, Access to Medicine Domain and Research issue. 2000-2010.

Classification/Categories	Frequency (N)	Percent* (%)
<i>Health System Levels</i>		
Health sector (policies or institutions)	41	35.34%
Health services delivery	30	25.86%
Patients, households and communities	28	24.14%
National policies or institutions cutting across sectors	11	9.48%
Regional and international policies and institutions	6	5.17%
<i>Domains</i>		
Leadership and governance	25	26.04%
Sustainable financing and affordability and price of medicines	22	22.92%
Medicines selection and use	21	21.88%
Availability of medicines	16	16.67%
Human resources for health	3	3.13%
Quality of medicines and quality and quality assurance systems	3	3.13%
Medicines information and information systems	2	2.08%
N/A	4	4.17%
<i>Research issue</i>		
Medicines Use	14	18.20%
Availability	13	16.90%
Medicines price/Affordability	11	14.30%
Financing model of medicines	10	13.00%
Health Litigation	9	11.70%
Policy implementation	9	11.70%
Multisource medicines/ Generics	8	10.40%
Legislation and regulation	5	6.50%
Good Pharmacy Practices	4	5.20%
IP related issues	4	5.20%
Evidence and health policy	3	3.90%
Methods	3	3.90%
Socioeconomic Determinants	3	3.90%
Health care and medicines seeking behavior	2	2.60%
Provision model of medicines	2	2.60%
Human resources for health	1	1.30%
Global policies and human rights	1	1.30%
Production of medicines	1	1.30%
Traditional medicine	1	1.30%

Categories are not mutually exclusive

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Access to Medicines in Latin America and the Caribbean (LAC): a scoping study

Running title: Scoping study on access to medicines

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Keywords: Access to medicines; Bibliometrics; Low and middle-income countries; Latin America; Caribbean region

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Abstract

Objective: To assess scientific publication trends on Access to Medicines (ATM) in Latin America and the Caribbean (LAC) low and middle income countries (LMIC) and to map research gaps, focusing on methodological approaches used to study ATM, institutions and countries involved as well as the main issues raised by authors.

Search strategy: A scoping study of the scientific literature on ATM was performed, on Medline, ISI, SCOPUS and Lilacs databases from 2000 to 2010.

Selection criteria: Research articles and reviews published in English, Spanish and Portuguese were included. Studies including only high-income countries were excluded, as well as those carried out in very limited settings and discussion papers.

Data extraction: The 77 articles retained were categorized through consensus among the research team according to the level of the health system addressed, ATM domain and research issues covered.

Results: Publications on ATM have increased over time during the study period (r 0.93, $p=0.00$; R^2 0.85). The top five countries covered were Brazil (68.8%), Mexico (15.6%), Colombia (11.7%), Argentina (10.4%) and Peru (10.4%). ‘Health services delivery’ and ‘Patients, household and communities’ were the health system levels most frequently covered. The ATM Domains ‘Leadership and governance’, ‘Sustainable financing, affordability and price of medicines’, ‘Medicines selection and use’ and ‘Availability of medicines’ were the top four explored. There are research gaps in important areas, such as ‘Human resources for health’, ‘Global policies and human rights’, ‘Production of medicines’ and ‘Traditional medicine’.

Conclusions: The upward trend on scientific publication reflects a growing research capacity in the region, which is concentrated on research teams in selected countries. The gaps on research capacity could be overcome through research collaboration among countries. It is important to strengthen these collaborations, assuring that interests and needs from the LMIC are addressed and local capacity building is promoted.

Key words Access to medicines; Bibliometrics; Scoping study; Low and middle-income countries; Latin America; Caribbean region.

ARTICLE SUMMARY

Article focus

- To identify methodological approaches and research issues which address access to medicines (ATM) in Latin American and the Caribbean (LAC) in the published literature.
- To learn about LAC researchers' capacity to produce evidence on ATM through articles published in peer-reviewed journals.
- To identify research gaps on ATM that should be addressed in future studies.
- To map potential opportunities for south-south collaboration on ATM research.

Key messages

- An increasing trend in scientific publications on ATM reflects a growing research capacity in LAC.
- Scientific publications in peer-reviewed journals are concentrated in few countries and focus on well-established areas and themes.
- 'Health services delivery' and 'Patients, household and communities' were the health system levels most frequently covered.
- The ATM Domains, 'Leadership and governance', 'Sustainable financing, affordability and price of medicines', 'Medicines selection and use' and 'Availability of medicines' were the top four explored.

Strengths and Limitations

- Local databases in Spanish and in Portuguese, the main languages in the region, which are generally not covered in other similar studies, were searched.
- A quality assessment of the papers retained was performed.

Introduction

Access to medicines (ATM) is a key component of health care systems. The provision of regular access to affordable, appropriate and high-quality medicines has been established as a global priority, highlighted in several international commitments such as World Health Assembly’s resolutions [1-4], Millennium Development Goals [5], UNGASS declarations [6 7], the Oslo Declaration [8] and the Political Declaration on HIV and AIDS: Intensifying Our Efforts to Eliminate HIV and AIDS [9]. In line with these commitments, governments of many Low and Middle Income Countries (LMIC) have implemented policies aimed at improving ATM.

Scaling-up ATM in low- and middle-income countries (LMIC) has been a major challenge faced by governments and health authorities. The delivery of medicines to most people in need depends on a series of efforts related to different access components or dimensions such as, sustainable financing, the existence of a network of reliable health services, and an efficient supply chain management [10].

In this context, the existence of reliable and accurate information on the different components of ATM is crucial for better decision-making. Despite the growing number of studies on issues like price and availability [11], quality data on access to and use of medicines are still lacking [12 13].

This work is part of activities carried out within the ATM policy research program, recently implemented by the Alliance for Health Policy and System Research (AHPSR) [14].

This paper aims to assess scientific publication trends on ATM in Latin America and the Caribbean (LAC) and to map research gaps.

Methods

A scoping study [15 16] of the scientific literature on ATM was performed covering ten years, from January 2000 to September 2010. This review intended to map scientific production on ATM related topics in LAC focusing on methodological approaches used to study ATM, institutions and countries involved as well as the main issues raised by authors.

Databases searched were Medline, ISI, SCOPUS and Lilacs, covering publications on ATM in the in the fields of health, social sciences and humanities. Search terms were set and combined according to the database features (Box 1).

The articles identified were screened and selected according to inclusion criteria, as follows: focus on ATM; addressing at least one LMIC at national or sub-national levels (districts, provinces, states); written in English, Spanish and Portuguese languages; abstract available; full-text available in open-access journals and on *Periódicos CAPES* e-journals database. Both and empiric and reviews articles were included. For review articles, some additional inclusion criteria applied: the article must include information on how the literature search was done and which scientifically recognized index was used; selection criteria must define the type of articles included in the review. Exclusion criteria were: studies including only high-income countries; empirical studies carried out in a very limited setting, such as hospitals or health centers. In all steps papers were reviewed and data extracted by two independent reviewers.

An exploratory analysis was performed taking into account the steps described below.

Articles retrieved were first sorted out according to the following variables: language; target population (general or disease specific), year of publication; type of study (empiric or review); first authors' country of residence and affiliation; countries covered.

Second, based on Bigdeli et al. [17], papers were categorized by level of the health system addressed: I) patients, households and communities; II) health services delivery; III) health sector (policies or institutions); IV) national policies or institutions cutting across sectors; and V) regional and international policies and institutions.

Third, they were classified according to ATM domains [18] as follows: a) medicines selection and use (consumption, rational use); b) sustainable financing, affordability and price of medicines; c) leadership and governance (policies formulation and implementation, legislation, health litigation); d) availability of medicines; e) human resources for health; f) quality of medicines and quality assurance systems'; g) medicines information and information systems.

Fourth, based on articles' research questions, research issues were identified and categorized by consensus among authors in nineteen categories related to each of the above ATM domains (Box 2)

Descriptive statistics (frequencies and percentages) were calculated to characterize distribution of papers according to the variables and categories mentioned above. Linear regression was performed to test the relationship between number of papers and year of publication. The strength and direction of this association was estimated by calculating the correlation coefficient (Pearson's r) and its statistical significance (p-value). Data linearity fit was expressed by coefficient of determination (R^2). Identified trends were depicted on scatter plots.

It was observed that a great part of papers retrieved covered Brazil and were produced by Brazilian authors. In order to avoid taking Brazilian production trends as the general one, data were stratified by countries covered (Brazil; LAC excluding Brazil; and multi-country studies) and first authors' country of residence (Brazil; LAC excluding Brazil; and EU / USA), when analyzing time trends.

Results

A total of 77 scientific articles were retained after the selection process as depicted in Figure 1.

Around half of the retained papers (53.7%) were published in English, 37.7% in Portuguese and 9.1% in Spanish. Most of them (72.7%) targeted general population. The majority of studies (85.7%) were empiric - quantitative and qualitative approaches were adopted in 58.4% and 22.1% respectively; mixed-methods were used in the remaining 19.5%.

Regarding first author's country of residence, Brazil was the leader (57.1%), followed by the United States of America (USA) (20.8%). First author's affiliation was linked to academic institutions in 76.6% of the papers.

The top five countries covered were Brazil (68.8%), Mexico (15.6%), Colombia (11.7%), Argentina (10.4%) and Peru (10.4%). This picture changes when multi-country studies are excluded and only studies covering a single country are considered: in such case, Brazil accounted for 55.8% of publications, while the above mentioned countries accounted for 6.5%, 3.9%, 1.3% and 3.9%, respectively.

First authors of the seventeen multi-country studies (22.1% out of 77) were mostly affiliated to institutions from the USA (8) and Brazil (5).

Multi-country studies were mostly published in English (94.1%), especially those covering LAC excluding Brazil. For studies covering Brazil the preferential language was Portuguese (65.1%).

When the first author's country of residence was Brazil, Portuguese was the most frequent language of publication (65.9%). In LAC countries, excluding Brazil, around half of the publications were in Spanish (55.6%) and when first author's country of residence was in the EU or the USA, English was the language of publication for all papers.

The number of publications related to ATM increased over time during the study period (Figure 2, A). The overall correlation (r) reflecting the association between the number of publications and year was 0.93 ($p=0.00$). The R^2 value 0.85 indicates a significant sustained increase over the 10 years covered by the study period. This increase refers mostly to publications covering Brazil as study setting (r 0.89, $p<0.01$, R^2 0.79 – Figure 2, B) and less extensively to those covering more than one country (r 0.69, $p<0.05$, R^2 0.48 – Figure 2C). The slight increase in the number of publications on ATM covering single LAC countries, excluding Brazil, however, shows little statistical significance (r 0.56, $p<0.10$, R^2 0.31 – Figure 2, D). The analysis by country of residence of the first author points out to similar trends, as can be observed in Figure 2E: publication with authors from Brazil responded for the higher growth rate (r 0.87, $p<0.01$, R^2 0.76), followed by those from high-income countries (r 0.78, $p<0.01$, R^2 0.61), and other LAC countries (r 0.59, $p<0.10$, R^2 0.34).

As Table 1 shows, 'Health sector', 'Health services delivery' and 'Patients, household and communities' were the three health system levels most frequently covered. The ATM Domains 'Leadership and governance', 'Sustainable financing, affordability and price of medicines', 'Medicines selection and use' and 'Availability of medicines' were the top four explored.

The top most researched issues were 'Medicines Use' (18.2%), 'Availability' (16.9%), 'Medicines price/Affordability' (14.3%), 'Financing model of medicines' and 'Health Litigation' (11.7%), 'Policy implementation' (11.7%) and Multisource medicines/Generics (10.4%).

Discussion

The growing trend in the production of papers related to ATM in LAC countries found in this study is consistent with the findings of other studies [12 13]. However Ritz *et al.* [13] report a steep increase in the number of papers in 2007, while this study shows a consistent trend of growth in Brazil’s production from 2000 to 2010. As previously mentioned, this production accounts for most of the general growth identified in America’s LMIC. This is consistent with an important and rapid growth of general scientific production in Brazil which been observed in the last decade, especially in the field of public health [19].

There are at least two main reasons to explain this picture. First, there has been a longstanding investment in capacity building for research in Brazil since mid 1970s. Second, since 2003 Brazilian government, among other initiatives, has been increasing funds and grants for scientific research in priority areas of knowledge, which includes public health [20 21]. Moreover, only five countries in the region have official health research priority agendas (Argentina, Brazil, Costa Rica, Paraguay and Peru) and only two of them (Brazil and Paraguay) explicitly include ATM issues [22].

The majority of papers published in Portuguese reflect the leadership of Brazil in the scientific production of LAC. This is also a consequence of the increasing public financing for research driven by Ministry of Health priorities. In this case, rather than focus on the dialogue with the international community of researchers, Brazilian authors gave priority to provide health authorities and national researchers with relevant information that can be used to promote improvements of the health system [19].

However, it is noteworthy that a trend in the growth of publications in English [23] was also observed, especially when multi-country studies were concerned. It reflects the interest of high-income countries’ authors in the implementation of ATM policies in the sub-region. This also indicates an effort developed by LAC researchers in order to contribute to the discussion of internationally relevant issues, which takes place mainly in English language peer-reviewed journals.

The choice for research method should be based on the research question and both qualitative and/or quantitative methods are acceptable. However, as the size of the effect is usually a crucial estimation, quantitative methods, particularly randomized clinical trials, have been preferred for producing evidence, including for social and health policy [24 25]. More

recently, the importance of qualitative approach has been increasingly recognized and used for health services and public health studies [26] This same pattern was observed in our study.

A smaller proportion of studies employing qualitative methods was found, which indicates the need for a better balance between quantitative and qualitative research, in order to reflect context specificities as well as to enhance policy learning [27 28]. The proportion of studies using mixed-methods may demonstrate the complexity of ATM issues, within the broader HPSR field, referred by Gilson *et al* 2011 [27] and Sheikh *et al* [28] who demand for interdisciplinary developments and a wide spectrum of methodologies.

Considering the Health System Levels, the most important point of discussion is the scarcity and small variety of issues addressed within Levels IV (national policies or institutions cutting across sectors) and V (Regional and international policies and institutions). This reflects the lack of attention in research that is given to: (a) national issues beyond the health sector and related to economy or trade, such as medicines production and legislation and regulation and (b) international issues, such as 'Global Policies' and 'Human Rights' and 'International Legislation'. The few publications found in level IV focused on litigation and court decisions while. the studies in Level V addressed intellectual property issues. These findings point to the importance of approaching ATM in broader national and international contexts.

Research gaps were identified in the domains of 'Human resources for health', 'Quality of medicines and quality and quality assurance systems', and 'Medicines information and information systems'. It is noteworthy that two of the most important health system building blocks [12], 'Human resources' and 'Health information', are under-represented in ATM research.

The categorization according to issues clearly shows concentration of publications in some, more traditional areas – 'Medicines Use', 'Availability', 'Medicines price/Affordability' and 'Financing model of medicines', directly related to the WHO ATM framework [10]. Meanwhile, there are research gaps in other important areas as 'Human resources for health', 'Global policies and human rights', 'Production of medicines' and 'Traditional medicine'.

Our study presents several limitations. Independently of the approach, the quality of studies is a critical issue to be considered, in order for the results to appropriately inform decision making [25 29]. However, as we aimed at a comprehensive scoping study rather than an in-

depth literature review no judgment on quality criteria was applied to papers retrieved and this aspect was not considered in the trends addressed.

Regarding the language criterion, which was used on initial search filters, it should be noted that only two countries in the region have different native languages from those included. This filter was therefore not considered as a significant bias.

Due to feasibility, open sources and the Brazilian academic public database – *Periódicos CAPES* – were used to recover full texts. This database is fairly broad (around 20,000 journals) and papers not available there or through other open sources are hardly accessible to researchers or policymakers in the region. Therefore, this was not considered a relevant bias in terms of availability of evidence to guide further research and decision-making.

Publications were assumed here as *proxys* of research production. However, barriers such as the acceptability of local approaches in high impact scientific journals, difficulties in scientific writing and writing in English [30] have a negative impact on the conversion of research findings in scientific communications.

Since “access to medicines” is not a Mesh term and the existing Mesh terms are not suitable, a broad range of terms were used in order to get the best possible coverage of relevant papers. Moreover by retaining only the available full text article, the results might be influenced by the “full text bias”.

Finally, despite the fact that the study covered a large period of 10 years, the search was limited to late 2010 and does not account for papers published in 2011 and 2012. This is a relative limitation as trends over time are analyzed and reveal significant changes over the past decade.

In conclusion, our study identified relevant scientific publication trends on ATM reflecting a growing research capacity in the region, but concentrated in few countries and research themes. This apparent gap on research capacity in many LMIC could be overcome through research collaboration among countries. Thus health research funders should promote this type of arrangement, to enhance and take advantage of the existing capacity, while fostering a more balanced development in the region. Also, a number of publications involving researchers and institutions from high-income countries was identified. It is important to strengthen this collaboration ensuring that interests and needs from the LMIC are addressed and local capacity building is promoted.

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The authors do not identify any competing interest related to this study.

Box 1 – Search strategy for scientific publication on access to medicines in Latin America and Caribbean syntax by Database. 2000-2010

Database	Search Strategy syntax	Note
Medline	("pharmaceutical preparations"[MeSH Terms] OR "drugs, essential"[MeSH Terms] OR "drugs, generic"[MeSH Terms]) AND ("health services accessibility"[MeSH Terms] OR "health policy"[MeSH Terms]) AND ("humans"[MeSH Terms] AND (English[lang] OR Spanish[lang] OR Portuguese[lang])) AND ("2000/01/01"[PDAT] : "2010/09/30"[PDAT])) AND ("humans"[MeSH Terms] AND (English[lang] OR Spanish[lang] OR Portuguese[lang])) AND ("2000/01/01"[PDAT] : "2010/09/30"[PDAT]))	Thesaurus exists These terms were identified with the support of an expert on bibliography search strategy.
Lilacs	<p>Portuguese ((Preparações Farmacêuticas) OR (Medicamentos Essenciais) OR (Medicamentos Genéricos)) AND ((Acesso aos serviços de saúde) OR (Política de Saúde)) em assunto (search for Mesh/Desc terms)</p> <p>Spanish ((Preparaciones Farmacéuticas) OR (Medicamentos <u>Esenciales</u>) OR (Medicamentos Genéricos)) AND ((Accesibilidad de los Servicios de Salud) OR (Política de Salud))</p> <p>English ((Pharmaceutical Preparations) OR (Drugs, Essential) OR (Drugs, Generic)) AND ((Health Services Accessibility) OR (Health Policy))</p>	
Scopus	(TITLE-ABS-KEY("access to medicines" OR "Medicines Price" OR "Rational use of medicine" OR "medicines affordability" OR "affordability of medicines" OR "accessibility of medicines" OR "medicines accessibility" OR "Medicines financing" OR "Availability of medicines" OR "medicines availability") AND SUBJAREA(mult OR agri OR bioc OR immu OR neur OR phar OR mult OR medi OR nurs OR vete OR dent OR heal OR mult OR arts OR busi OR deci OR econ OR psyc OR soci) AND PUBYEAR AFT 1999 AND PUBYEAR BEF 2011)	Thesaurus does not exist These terms came from the guiding template proposed by AHPSR, 2012. [18]
ISI	Topic=(access to medicines OR "Medicines Price" OR "Rational use of medicines" OR "medicines affordability" OR "affordability of medicines" OR "accessibility of medicines" OR "medicines accessibility" OR "Medicines financing" OR "Availability of medicines" OR "medicines availability") Refined by: Languages=(ENGLISH OR PORTUGUESE OR SPANISH) AND Publication Years=(2010 OR 2003 OR 2009 OR 2004 OR 2008 OR 2001 OR 2007 OR 2000 OR 2006 OR 2005)	

Box 2 –Categories related to ATM domains

<i>Categories</i>
Medicines Use
Availability
Medicines price/Affordability
Financing model of medicines
Health Litigation
Policy implementation
Multisource medicines/ Generics
Legislation and regulation
Good Pharmacy Practices
IP related issues
Evidence and health policy
Methods
Socioeconomic Determinants
Health care and medicines seeking behavior
Provision model of medicines
Human resources for health
Global policies and human rights
Production of medicines
Traditional medicine

Figure 1. Stepwise process for selection of papers concerning access to medicines in Latin America and Caribbean. 2000-2010.

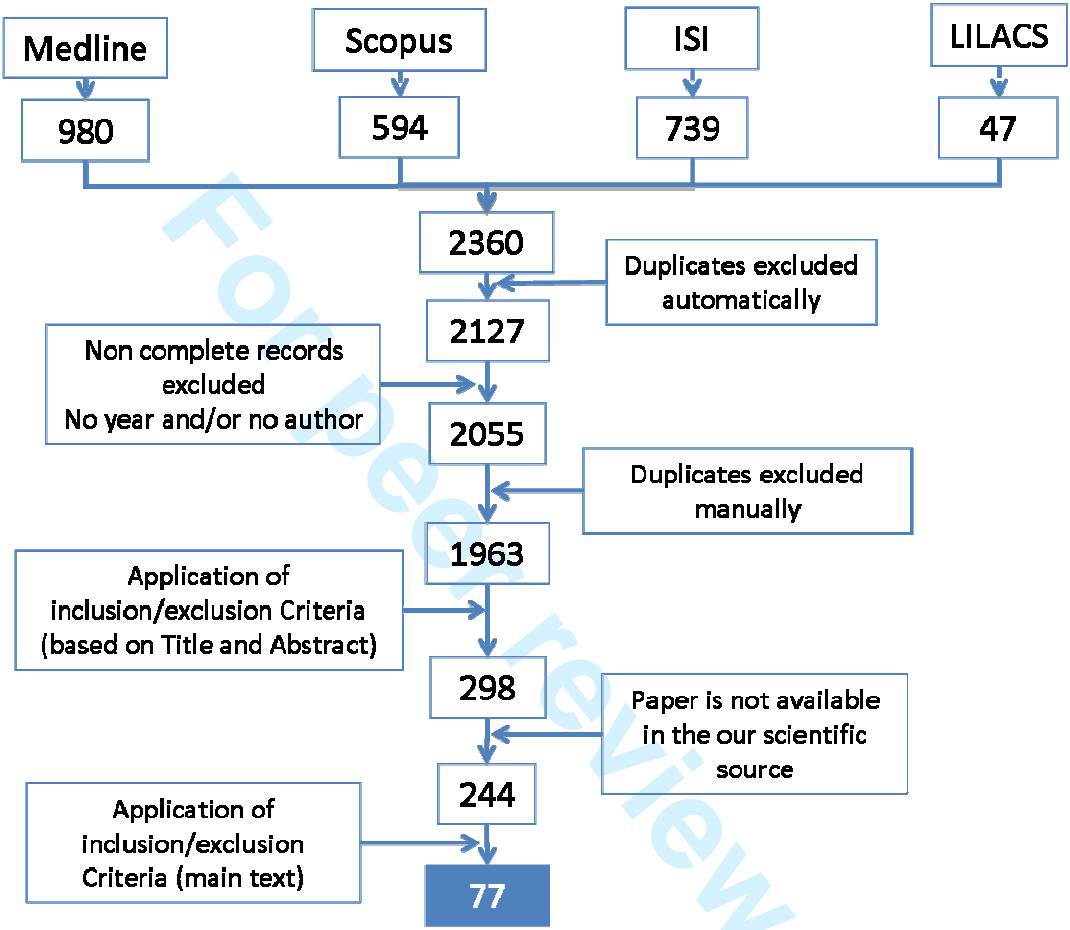


Figure 2. Number of papers related to access to medicines in Latin America and Caribbean per year by country covered and first author's country of residence, 2000 – 2010.

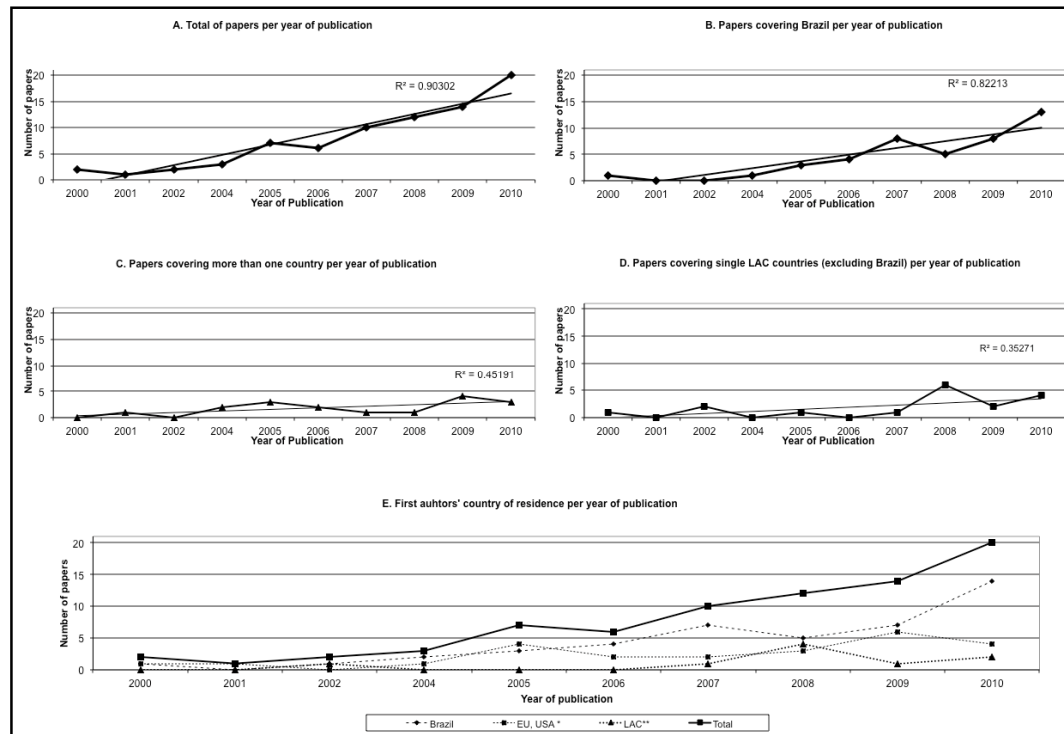


Table 1. Distribution of papers by Health System Level, Access to Medicine Domain and Research issue. 2000-2010.

Classification/Categories	Frequency (N)	Percent* (%)
<i>Health System Levels</i>		
Health sector (policies or institutions)	41	35.34%
Health services delivery	30	25.86%
Patients, households and communities	28	24.14%
National policies or institutions cutting across sectors	11	9.48%
Regional and international policies and institutions	6	5.17%
<i>Domains</i>		
Leadership and governance	25	26.04%
Sustainable financing and affordability and price of medicines	22	22.92%
Medicines selection and use	21	21.88%
Availability of medicines	16	16.67%
Human resources for health	3	3.13%
Quality of medicines and quality and quality assurance systems	3	3.13%
Medicines information and information systems	2	2.08%
N/A	4	4.17%
<i>Research issue</i>		
Medicines Use	14	18.20%
Availability	13	16.90%
Medicines price/Affordability	11	14.30%
Financing model of medicines	10	13.00%
Health Litigation	9	11.70%
Policy implementation	9	11.70%
Multisource medicines/ Generics	8	10.40%
Legislation and regulation	5	6.50%
Good Pharmacy Practices	4	5.20%
IP related issues	4	5.20%
Evidence and health policy	3	3.90%
Methods	3	3.90%
Socioeconomic Determinants	3	3.90%
Health care and medicines seeking behavior	2	2.60%
Provision model of medicines	2	2.60%
Human resources for health	1	1.30%
Global policies and human rights	1	1.30%
Production of medicines	1	1.30%
Traditional medicine	1	1.30%

Categories are not mutually exclusive

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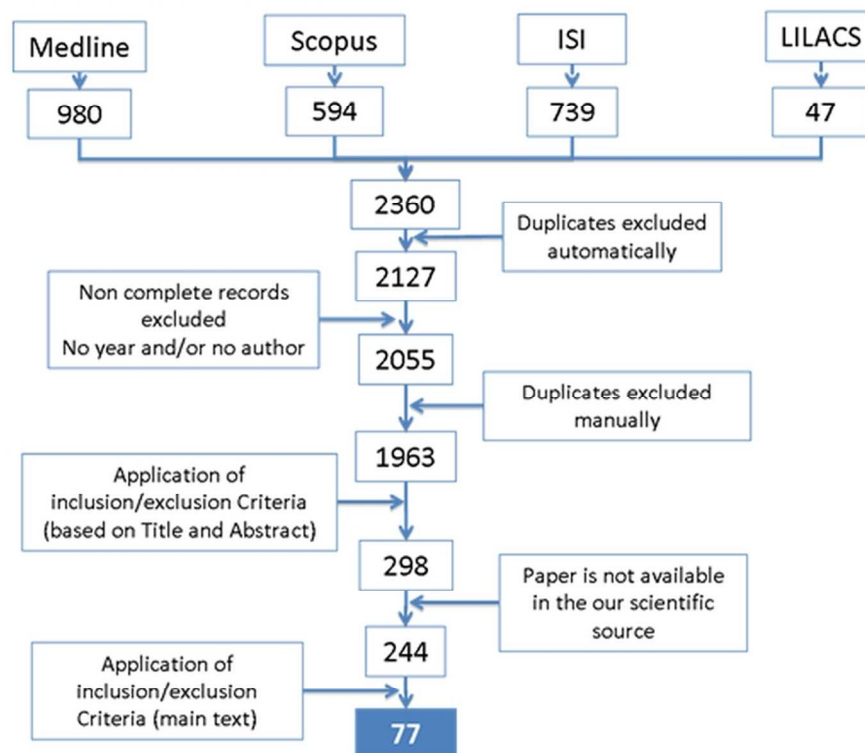
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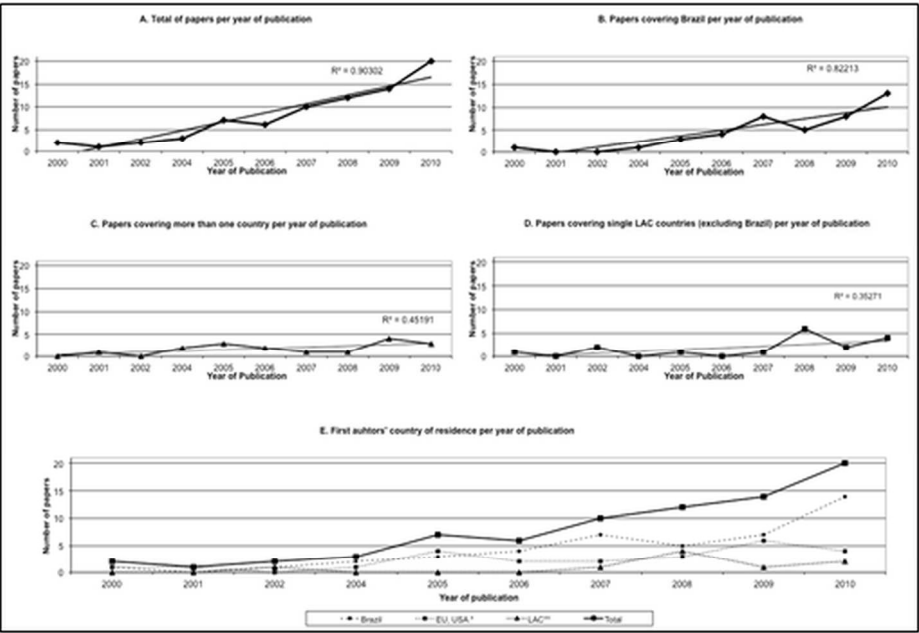
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Figure 1. Stepwise process for selection of papers concerning access to medicines in Latin America and Caribbean. 2000-2010.



103x90mm (300 x 300 DPI)

Figure 2. Number of papers related to access to medicines in Latin America and Caribbean per year by country covered and first author's country of residence, 2000 – 2010.



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